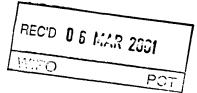
P. ENT COOPERATION TREAT

•	From the INTERNATIONAL BUREAU		
PCT	To:		
NOTIFICATION OF ELECTION	Assistant Commissioner for Patents		
(PCT Rule 61.2)	United States Patent and Trademark Office		
(FCT hule 01.2)	Box PCT		
	Washington, D.C.20231		
	ETATS-UNIS D'AMERIQUE		
Date of mailing (day/month/year) 28 July 2000 (28.07.00)	in its capacity as elected Office		
	Applicant's or agent's file reference		
International application No. PCT/JP99/06943	PWO-19119		
International filing date (day/month/year) 10 December 1999 (10.12.99)	Priority date (day/month/year) 14 December 1998 (14.12.98)		
Applicant			
TAKE, Kazuhiko et al			
1. The designated Office is hereby notified of its election mad	e:		
X in the demand filed with the International Preliminary	y Examining Authority on:		
31 May 2000 (
in a notice effecting later election filed with the Intere	national Bureau on:		
			
2. The election X was			
) [
was not			
made before the expiration of 19 months from the priority	date or, where Rule 32 applies, within the time limit under		
Rule 32.2(b).			
	·		
•			
•			
The International Bureau of WIPO	Authorized officer		
34, chemin des Colombettes	Maria Kirchner		
1211 Geneva 20, Switzerland	Telephone No.: (41-22) 338.83.38		
Facsimile No.: (41-22) 740.14.35	10.00.10.10.10.10.10.10.100.00		









(PCT Article 36 and Rule 70)

	or agent's fil	e reference	FOR FURTHER ACTION		otification of Transmittal of International inary Examination Report (Form PCT/IPEA/416)
PWO-19	119				
	al application	No.	International filing date (day/mo	nth/year)	Priority date (day/month/year)
PCT/JP9	,		10/12/1999		14/12/1998
Internationa C07D413		ssification (IPC) or i	national classification and IPC		
Applicant FUJISAV	VA PHARI	MACEUTICAL (CO., LTD. et al.		
1. This i	nternationa s transmitte	d preliminary exa d to the applicant	mination report has been preparaction according to Article 36.	red by this	International Preliminary Examining Authority
2. This I	REPORT c	onsists of a total of	of 6 sheets, including this cove	r sheet.	
b (:	een amend see Rule 7	led and are the b	asis for this report and/or shee 607 of the Administrative Instru	s containir	iption, claims and/or drawings which have ng rectifications made before this Authority ler the PCT).
3. This i		ains indications re	lating to the following items:		
Н	☐ Prio	rity			
HI	⊠ Non	establishment of	opinion with regard to novelty,	inventive	step and industrial applicability
IV	☐ Laci	of unity of inven	tion		
V			under Article 35(2) with regard tions suporting such statement	to novelty,	inventive step or industrial applicability;
VI	⊠ Cert	ain documents o	ited		
VII	☐ Cert	ain defects in the	international application		
VIII	⊠ Ceri	ain observations	on the international application		
Date of sub	omission of t	ne demand	Date	of completion	on of this report
31/05/20	00		01.0	3.2001	
	examining a	•	nal Auth	orized office	OF CONTROL OF THE CON
<u>@</u>)	D-80298 N	Patent Office Iunich 9 2399 - 0 Tx: 5236	Gos 56 epmu d	s, I	
		9 2399 - 4465	'	shana Na .	40 80 2300 8202

International application No. PCT/JP99/06943

ļ.	Bas	sis fth report	
1.	resp the	oonse to an invitatio	rawn on the basis of (substitute sheets which have been furnished to the receiving Office in on under Article 14 are referred to in this report as "originally filed" and are not annexed to not contain amendments (Rules 70.16 and 70.17).):
	1-23	31	as originally filed
	Clai	ims, No.:	
	1-10)	as originally filed
2.	With lang	n regard to the lang guage in which the i	puage, all the elements marked above were available or furnished to this Authority in the nternational application was filed, unless otherwise indicated under this item.
	The	se elements were a	available or furnished to this Authority in the following language: , which is:
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pu	iblication of the international application (under Rule 48.3(b)).
		the language of a 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule
3.			eleotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:
		contained in the in	ternational application in written form.
		filed together with	the international application in computer readable form.
		furnished subsequ	ently to this Authority in written form.
		furnished subsequ	ently to this Authority in computer readable form.
			t the subsequently furnished written sequence listing does not go beyond the disclosure in pplication as filed has been furnished.
		The statement tha listing has been fu	t the information recorded in computer readable form is identical to the written sequence rnished.
4.	The	amendments have	e resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:
		the drawings,	sheets:
5.		This report has be	en established as if (some of) the amendments had not been made, since they have been

considered to go beyond the disclosure as filed (Rule 70.2(c)):

International application No. PCT/JP99/06943

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6.	Add	litional observations, if ne	ecessar	y:	
III.	Nor	n-establishment of opin	ion with	n regard	to novelty, inventive step and industrial applicability
1.					appears to be novel, to involve an inventive step (to be non- e not been examined in respect of:
		the entire international a	application	on.	
	×	claims Nos. 8.			
be	caus	se:			
	☒	the said international ap not require an internatio see separate sheet			said claims Nos. 8 relate to the following subject matter which does examination (<i>specify</i>):
		the description, claims of that no meaningful opinion			cate particular elements below) or said claims Nos. are so unclear ned (specify):
		the claims, or said claim could be formed.	ns Nos.	are so in	nadequately supported by the description that no meaningful opinion
		no international search	report h	as been e	established for the said claims Nos
2.	and				ination report cannot be carried out due to the failure of the nucleotidgy with the standard provided for in Annex C of the Administrative
		the written form has not	been fu	ırnished d	or does not comply with the standard.
		the computer readable f	form has	s not bee	en furnished or does not comply with the standard.
٧.		asoned statement unde stions and explanations			vith regard to novelty, inventive step or industrial applicability; ch statement
1.	Stat	tement			
	Nov	velty (N)	Yes: No:	Claims Claims	
	Inve	entive step (IS)	Yes: No:	Claims Claims	
	Indu	ustrial applicability (IA)	Yes:	Claims	1-9,10

International application No. PCT/JP99/06943

No: Claims 8

2. Citations and explanations see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet



INTERNATIONAL PRELIMINARY Internation EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/JP99/06943

Priority

The priority document pertaining to the present application has not been checked at the time of establishing this preliminary examination report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document WO 98 57954 cited in the international search report could become relevant to assess whether claim 1 (and dependent claims thereon) satisfies the criteria set forth in Article 33(1) PCT.

Novelty

D2: WO 97 22597 describes compounds which do not fall within the scope of the subject-matter claimed mainly in view of the proviso introduced at the end of claim 1. However, it should be pointed out that the novelty of an invention whose subject-matter is a choice among a known group depends on whether the choice adduces a teaching of a technical nature not contained in the state of the art. The Examiner could not find wherein the structural distinction between D2 and the claimed subject-matter exactly resides.

Novelty cannot be recognized.

Inventive step

The problem underlying the present application appears to reside in the provision of further piperazine derivatives which have pharmacological activities such as Tachykinin antagonism.

D2 as well as D3: WO 97 08166 A both describe structurally very closely related compounds (see also under novelty) also useful as Tachykinin antagonists or more specifically neurokinin antagonists (D3). Data are given on pages 28 to 31 and 49 to 55 respectively.

The solution of the problem underlying the present application has to be seen in the provision of the derivatives according to claim 1 which, however, do not show any particular novelty rendering feature and for which no quantitative data could be found.

It appears that the problem as stated above has been already solved by the compounds claimed in D2.

Therefore in view of this objection above, the compounds claimed do not represent a solution to the problem stated supra since no unexpected effects or advantages which were not derivable from the teaching of the highly relevant document D2 were shown.



INTERNATIONAL PRELIMINARY International application No. PCT/JP99/06943 EXAMINATION REPORT - SEPARATE SHEET

Always in the case of a selection invention, the structural distinguishing portion must be responsibly for the unforeseeable effects on which an inventive step could be recognized.

No inventive step can be acknowledged.

Clarity

The term "aryl further substituted" used in claim 1, is considered to be non-limitative and embraces an infinite number of possibilities not yet explored by the Applicant; it should have been limited to the specific meanings given in the description page 8, as otherwise it is difficult to ascertain if the problem has been indeed solved by all the compounds claimed considered as obvious modifications or equivalents to one or more particular examples.

The expression "lower" used in the claims (for many substituents like i.a. alkyl, alkenyl or alkoxyl) is considered to be unclear in scope, since it does not precisely define the matter for which protection is sought, specially the upper limit (being in this case sometimes different from group to group).

Industrial applicability

For the assessment of the present claims 8 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		of Transmittal of International Search Report 20) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/JP 99/06943	10/12/1999	14/12/1998
Applicant		
FUJISAWA PHARMACEUTICAL C	O., LTD. et al.	•
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Auth ansmitted to the International Bureau.	nority and is transmitted to the applicant
This International Search Report consists It is also accompanied by	of a total of sheets. a copy of each prior art document cited in this	report.
1. Basis of the report		
	international search was carried out on the bas ess otherwise indicated under this item.	sis of the international application in the
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of the	he international application furnished to this
was carried out on the basis of the	e sequence listing :	sternational application, the international search
	nal application in written form. rnational application in computer readable form	n
	this Authority in written form.	
	this Authority in computer readble form.	
	osequently furnished written sequence listing do s filed has been furnished.	oes not go beyond the disclosure in the
the statement that the info furnished	ormation recorded in computer readable form is	s identical to the written sequence listing has been
2. Certain claims were fou	nd unsearchable (See Box I).	
3. Unity of invention is lac	king (see Box II).	
4. With regard to the title,		
X the text is approved as su	bmitted by the applicant.	
the text has been establis	hed by this Authority to read as follows:	
5. With regard to the abstract,		
the text is approved as su		
	hed, according to Rule 38.2(b), by this Authorit date of mailing of this international search rep	
6. The figure of the drawings to be publ	ished with the abstract is Figure No.	
as suggested by the appli	cant:	X None of the figures.
because the applicant fail	· · · · · · · · · · · · · · · · · · ·	
because this figure better	characterizes the invention.	



		P	P 99/0	5943
IPC 7	CO7D495/04 CO7F7/18 A61K31/	3/06 C07D471/0 /535 A61K31/49 0413/06,265:00,2	5 A61P29	- •
	SEARCHED	ication and IPC		
	Cumentation searched (classification system followed by classification	ation symbols)		
IPC 7	CO7D CO7F			
	ion searched other than minimum documentation to the extent that	•		ned
Electronic d	ata base consulted during the international search (name of data b	ease and, where practical, se	arch terms used)	
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT			,
Category °	Citation of document, with indication, where appropriate, of the re-	elevant passages		Relevant to claim No.
Ρ,Χ	WO 98 57954 A (NAKAI KAZUO ;TAKE (JP); AZAMI HIDENORI (JP); EIKYU 23 December 1998 (1998-12-23) claims 1-4,6,7,9,10; examples 6	YOSHIT)		1-3,6,7, 9,10
X	WO 97 22597 A (FUJISAWA PHARMACE; MATSUO MASAAKI (JP); MANABE TAK 26 June 1997 (1997-06-26) claims 1-8,10,11,14; examples 2	ASHI (J)		1-3,6,7, 9,10
х	WO 97 08166 A (SCHERING CORP) 6 March 1997 (1997-03-06) claims 1-3,5,12-14			1-3,9,10
A	EP 0 655 442 A (FUJISAWA PHARMAC CO) 31 May 1995 (1995-05-31) claims 1-3,6-8; table 1	EUTICAL		1-3,9,10
<u> </u>	er documents are listed in the continuation of box C.	X Patent family men	nbers are listed in an	nex.
"A" documer conside "E" earlier de filing da "L" documen which is citation "O" documer other m "P" documer later tha	at which may throw doubts on priority claim(s) or scited to establish the publication date of another or other special reason (as specified) nt referring to an oral disclosure, use, exhibition or	"T" later document publishe or priority date and no cited to understand the invention "X" document of particular cannot be considered involve an inventive st "Y" document of particular cannot be considered document is combined ments, such combination the art. "&" document member of the invention of the inventi	t in conflict with the apprinciple or theory relevance; the claime novel or cannot be cep when the docume relevance; the claime to involve an inventive twith one or more of ion being obvious to me same patent family	application but underlying the ed invention onsidered to ent is taken alone ed invention exercises when the her such docu—a person skilled
8	May 2000.	12/05/200		
Name and ma	ailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer		

2



International Application No

A. CLASSIFI IPC 7	CATION OF SUBJECT MATTER (C07D401/06,241:00,213:00),(C07D40),(C07D40),(C07D413/14,265:00,241:00,207:00)	03/06,241:00,231:00),	
According to I	nternational Patent Classification (IPC) or to both national classific	ation and IPC	
B. FIELDS S			-
Minimum docu	umentation searched (classification system followed by classificati	on symbols)	
Documentatio	n searched other than minimum documentation to the extent that s	such documents are included in the fields so	earched
Electronic data	a base consulted during the international search (name of data ba	se and, where practical, search terms used	
C. DOCUMEN	ITS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the rel	evant passages	Relevant to claim No.
Further	documents are listed in the continuation of box C.	χ Patent family members are listed	in annex.
"A" document considere "E" earlier doc filing date "L" document which is a citation or "O" document other mea document later than	which may throw doubts on priority claim(s) or cited to establish the publication date of another r other special reason (as specified) referring to an oral disclosure, use, exhibition or ans published prior to the international filing date but	"T" later document published after the inte or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the do "Y" document of particular relevance; the cannot be considered to involve an indocument is combined with one or ments, such combined with one or ments, such combination being obvior in the art. "&" document member of the same patent	the application but every underlying the claimed invention be considered to cument is taken alone claimed invention ventive step when the ore other such docu- us to a person skilled
	ling address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer GOSS, I	·

2

nform on patent family members

International Application No PC 99/06943

Patent document cited in search repo		Publication date		Patent family member(s)	Publication date
WO 9857954	Α	23-12-1998	AU	7675098 A	04-01-1999
500,50	,,	20 12 1770	EP	0993457 A	19-04-2000
			ZA	9805255 A	06-01-1999
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			EP	0873320 A	28-10-1998
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			EP	0823906 A	18-02-1998
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EP 0655442	Α	31-05-1995	AU	689504 B	02-04-1998
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			US	5670505 A	23-09-1997
			US	5883098 A	16-03-1999
			ZA	9409228 A	01-08-1995
			BR	9500539 A	31-10-1995



From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

TABUSHI, Eiji Fujisawa Pharmaceutical Co., Ltd. Osaka Factory 1-6, Kashima 2-chome Yodogawa-ku, Osaki-shi Osaka 532-8514 **JAPON**

Date of mailing (day/month/year) 29 February 2000 (29.02.00)	
Applicant's or agent's file reference PWO-19119	IMPORTANT NOTIFICATION
International application No. PCT/JP99/06943	International filing date (day/month/year) 10 December 1999 (10.12.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 14 December 1998 (14.12.98)

- FUJISAWA PHARMACEUTICAL CO., LTD. et al
- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
14 Dece 1998 (14.12.98)	PP7706		21 Janu 2000 (21.01.00)
21 Octo 1999 (21.10.99)	PQ3568		21 Janu 2000 (21.01.00)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Marc Salzman

Telephone No. (41-22) 338.83.38



რ031360

Facsimile No. (41-22) 740.14.35

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

TABUSHI, Eiji
Fujisawa Pharmaceutical Co., Ltd.
Osaka Factory
1-6, Kashima 2-chome
Yodogawa-ku, Osaki-shi
Osaka 532-8514
JAPON

Date of mailing (day/month/year) 22 June 2000 (22.06.00)

Applicant's or agent's file reference

PWO-19119

IMPORTANT NOTICE

International application No. PCT/JP99/06943

International filing date (day/month/year) 10 December 1999 (10.12.99) Priority date (day/month/year)
14 December 1998 (14.12.98)

Applicant

FUJISAWA PHARMACEUTICAL CO., LTD. et al

 Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice: AU,CN,JP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,BO,BL,SD,SE,SC,SL,SL,SL,T,LTM,TB,TT,LIA,LIG,LIZ,VN,YL,ZA,ZW

RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 22 June 2000 (22.06.00) under No. WO 00/35915

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switz rland Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

1211 Geneva 20, Switz rlar Facsimile No. (41-22) 740.14.35

12.7.-5

Continuation of Form PCT/IB/308 NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

IMPORTANT NOTICE	
International application No. PCT/JP99/06943	

The applicant is hereby notified that, at the time of establishment of this Notice, the time limit under Rule 46.1 for making amendments under Article 19 has not yet expired and the International Bureau had received neither such amendments nor a declaration that the applicant does not wish to make amendments.